

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

**1-5. (canceled).**

**6. (currently amended):** A method for digesting a protein highly resistant to denaturation and degradation, comprising the step of bringing the protein highly resistant to denaturation and degradation into contact with an enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation and having the following properties:

- (a) activity and substrate specificity: hydrolyzing a peptide bond of a protein highly resistant to denaturation and degradation;
- (b) molecular weight: 31,000 (determined by an SDS-polyacrylamide gel electrophoresis using a homogeneous gel having a gel concentration of 12%);
- (c) isoelectric point: pI 9.3 (determined by polyacrylamide gel isoelectric focusing electrophoresis);
- (d) optimum pH: pH 9.0 to 10.0; and
- (e) optimum temperature for activity: 60 to 70°C,  
wherein the contacting step is carried out without preheating the protein.

**7-8. (canceled).**

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**9.** **(currently amended):** A method for detoxifying a pathogenic prion protein, comprising the step of bringing a subject which may be contaminated with a pathogenic prion protein into contact with an enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation and having the following properties:

- (a) activity and substrate specificity: hydrolyzing a peptide bond of a protein highly resistant to denaturation and degradation;
- (b) molecular weight: 31,000 (determined by an SDS-polyacrylamide gel electrophoresis using a homogeneous gel having a gel concentration of 12%);
- (c) isoelectric point: pI 9.3 (determined by polyacrylamide gel isoelectric focusing electrophoresis);
- (d) optimum pH: pH 9.0 to 10.0; and
- (e) optimum temperature for activity: 60 to 70°C,  
wherein the contacting step is carried out without preheating the subject.

**10.** **(canceled).**

**11.** **(previously presented):** The method according to claim 9, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**12-16. (canceled).**

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**17. (previously presented):** The method according to claim 6, wherein the enzyme has the following property:

(g) exhibiting an activity of 2 U/g or more as the activity of digesting a protein highly resistant to denaturation and degradation which is determined as an activity of digesting keratin azure.

**18. (previously presented):** The method according to claim 6, wherein the enzyme has the following property:

(h) derived from a microorganism belonging to genus *Bacillus*.

**19. (previously presented):** The method according to claim 6, wherein the enzyme is selected from the group consisting of

(X) an enzyme comprising the amino acid sequence of SEQ ID NO: 2;  
(Y) a modified enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation, and comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, or added in the amino acid sequence of SEQ ID NO: 2; and  
(Z) a homologous enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation, and comprising an amino acid sequence having an 85% or more homology with the amino acid sequence of SEQ ID NO: 2.

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**20.** **(previously presented):** The method according to claim 6, wherein the protein highly resistant to denaturation and degradation is a pathogenic prion protein.

**21.** **(canceled).**

**22.** **(previously presented):** The method according to claim 6, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**23.** **(canceled).**

**24.** **(previously presented):** The method according to claim 17, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**25.** **(canceled).**

**26.** **(previously presented):** The method according to claim 18, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**27.** **(canceled).**

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**28. (previously presented):** The method according to claim 19, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**29. (canceled).**

**30. (previously presented):** The method according to claim 20, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**31. (previously presented):** The method according to claim 9, wherein the enzyme has the following property:

(g) exhibiting an activity of 2 U/g or more as the activity of digesting a protein highly resistant to denaturation and degradation (determined as an activity of digesting keratin azure).

**32. (previously presented):** The method according to claim 9, wherein the enzyme has the following property:

(h) derived from a microorganism belonging to genus *Bacillus*.

**33. (previously presented):** The method according to claim 9, wherein the enzyme is selected from the group consisting of  
(X) an enzyme comprising the amino acid sequence of SEQ ID NO: 2;

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

(Y) a modified enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation, and comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, or added in the amino acid sequence of SEQ ID NO: 2; and

(Z) a homologous enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation, and comprising an amino acid sequence having an 85% or more homology with the amino acid sequence of SEQ ID NO: 2.

**34. (previously presented):** The method according to claim 9, wherein the protein highly resistant to denaturation and degradation is a pathogenic prion protein.

**35. (canceled).**

**36. (previously presented):** The method according to claim 31, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**37. (canceled).**

**38. (previously presented):** The method according to claim 32, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**39. (canceled).**

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**40.**     (**previously presented**): The method according to claim 33, wherein the contacting step is carried out without preheating the subject at 90°C or more.

**41.**     (**canceled**).

**42.**     (**previously presented**): The method according to claim 34, wherein the contacting step is carried out without preheating the subject at 90°C or more.